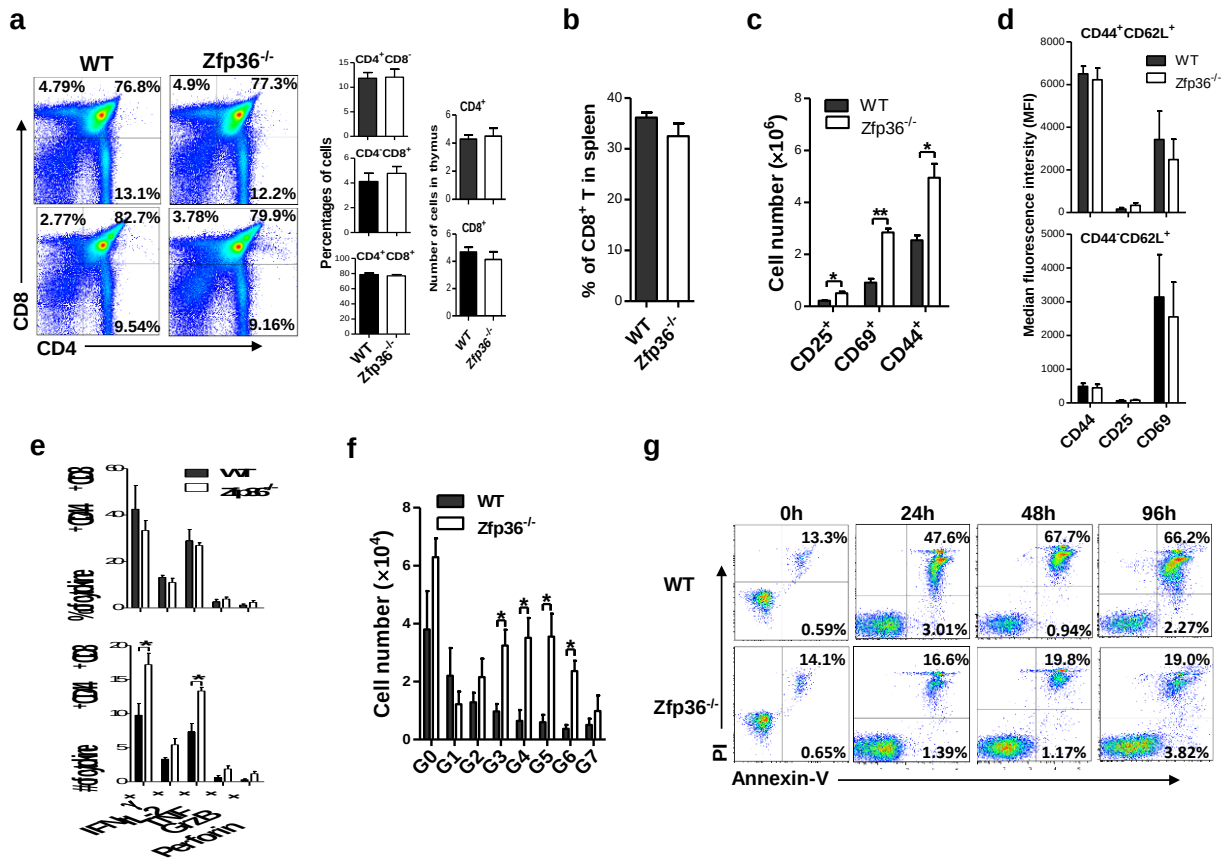
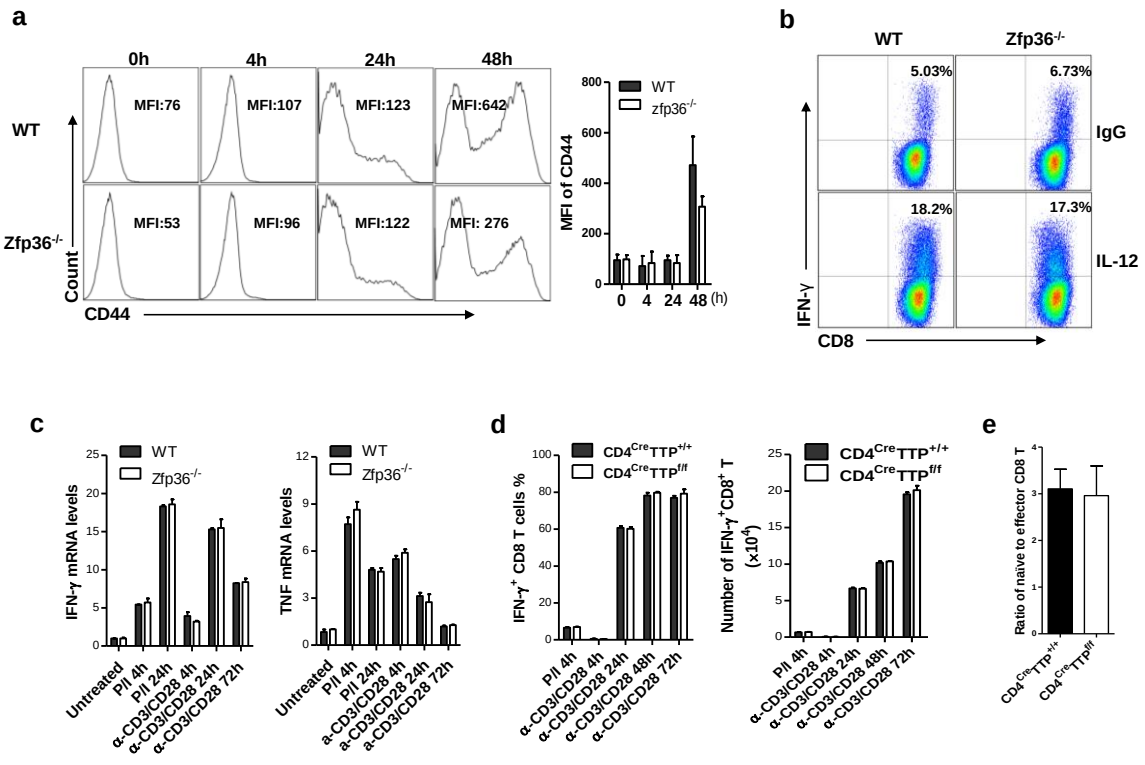


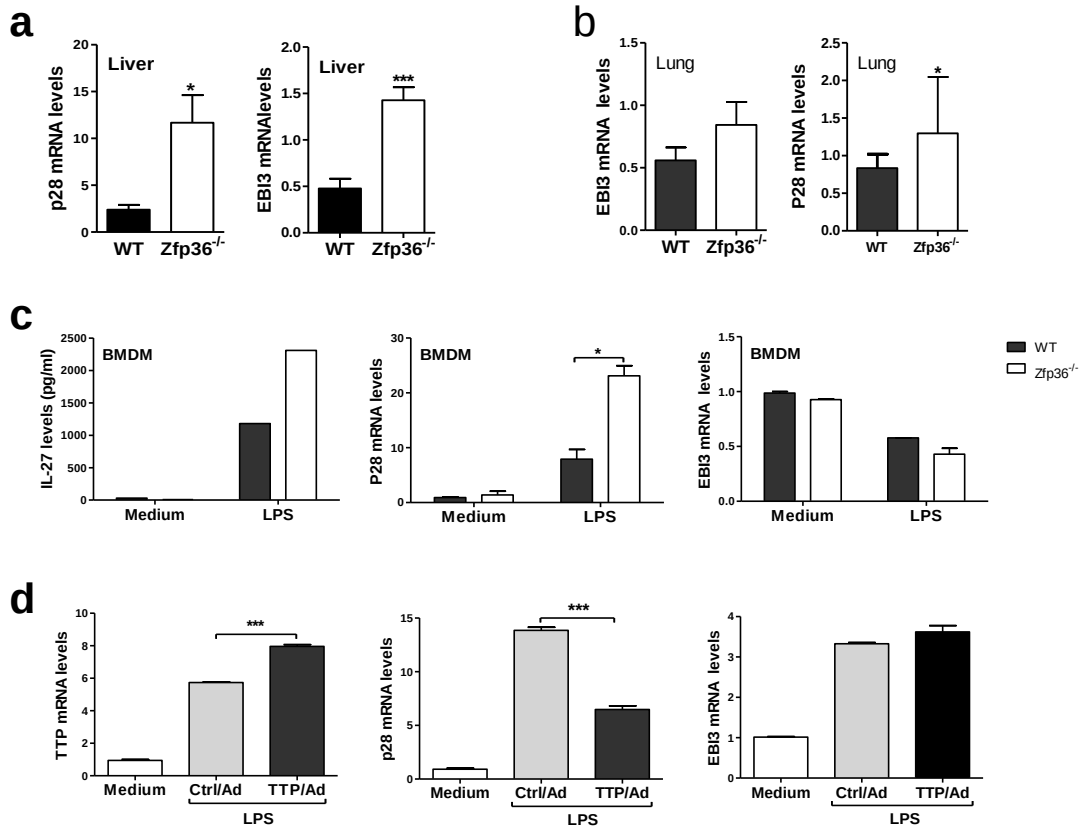

**Supplementary Fig. 1. TTP deficiency promotes proliferation, survival and activation of CD8$^+$ T cells.** (**a**) Thymocytes of female *Zfp36*$^{-/-}$ and WT littermates aged 6-8 weeks old were stained by anti-CD4 and CD8 antibodies, followed by detection by FACS gated on total thymocytes. The percentages of CD4$^+$, CD8$^+$ and CD4$^+$CD8$^+$ T cells as well as the numbers of CD4$^+$ and CD8$^+$ T cells in thymus were summarized as means ± s.d. from three pairs of mice. (**b**) Splenocytes from the above mice were stained by anti-CD3 and CD8 antibodies. The percentages of CD8$^+$ T cells in spleen were determined with FACS by gating on CD3$^+$ cells (n=6). (**c**) Splenocytes were isolated from female *Zfp36*$^{-/-}$ mice and WT littermates at 6 weeks old, and stained with antibodies against CD3, CD8, CD44, CD25, CD69 and CD62L. The CD25$^+$, CD69$^+$, CD44$^+$ and CD62L$^+$ CD8 T cells were detected with FACS gated on CD3$^+$CD8$^+$ double positive cells. The absolute numbers were calculated from three pairs of mice and

analyzed with unpaired student's *t* test. (**d**) The levels of CD44, CD25 and CD69 as in (c) were detected by FACS in $CD3^+CD8^+$ double positive cells. The median fluorescence intensities of CD44, CD25 and CD69 in $CD44^+CD62L^+$ and $CD44^-CD62L^+$ cells were calculated and summarized as means ± s.d. with three mice in each group. (**e**) The splenocytes as in (c) were stimulated by PMA and Ionomycin in the presence of GolGistop for 4 h, then intracellular IFN-γ, IL-2, TNF, Granzyme B and Perforin positive cells were detected with their respective antibodies, gated on CD44 in $CD3^+$ and $CD8^+$ double positive cells. Cytokine production was detected in the $CD44^+$ cells. Quantitative data represent means ± s.d. of $cytokine^+CD8^+$ T cells from three pair of mice. (**f**) Naïve CD8 T cells isolated from spleens of WT and *Zfp36*$^{-/-}$ mice were labeled by CFSE and stimulated by plate-coated α-CD3/CD28 Abs (1 μg/ml) for 72 h. Then proliferative generations were analyzed based on CFSE levels. Quantitative data represent means ± s.d. from three independent experiments. G represents generation. (**g**) Naïve CD8 T cells of WT and *Zfp36*$^{-/-}$ mice were stimulated by plate-coated α-CD3/CD28 Abs (1 μg/ml) for different times. PI and Annexin-V expression were detected with FACS by gating on $CD3^+CD8^+$ cells. Data represent one of three experiments with similar results. *: $p<0.05$; **: $p<0.01$; ***: $p<0.001$ between WT and *Zfp36*$^{-/-}$ groups.

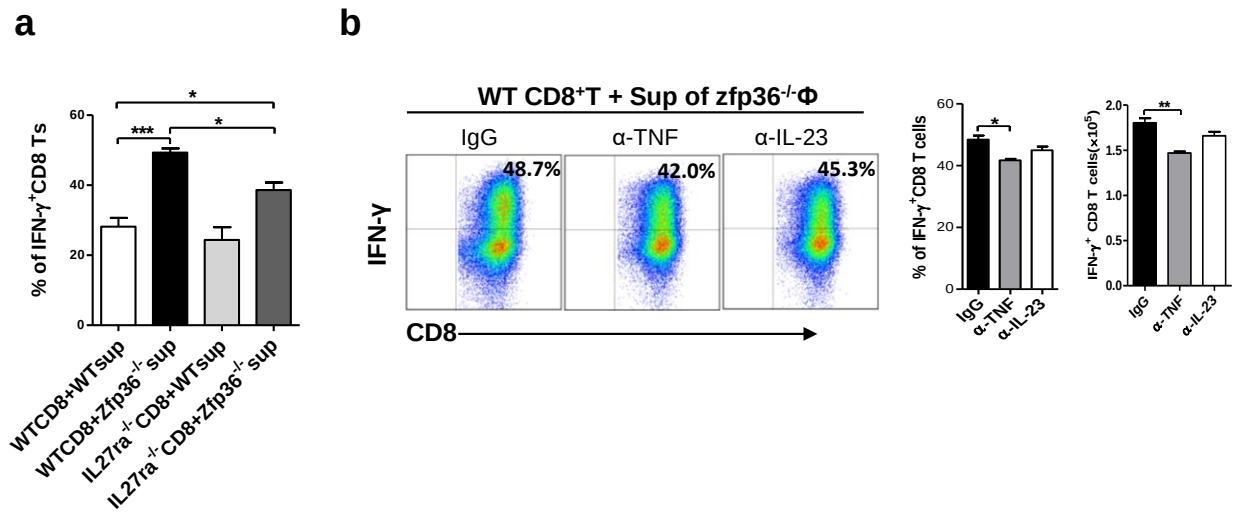



**Supplementary Fig. 2. TTP has no intrinsic effects on IFN-γ production by CD8$^+$ T cells.** (**a**) Naïve CD8$^+$ T cells isolated from WT and *Zfp36*$^{-/-}$ mice were stimulated with plate-coated α-CD3 and soluble α-CD28 Abs (1 μg/ml), then CD44 was detected at different times. Median fluorescence intensity (MFI) was shown as histogram and summarized from three experiments (means ± s.d.). (**b**) Naïve CD8 T cells from WT and *Zfp36*$^{-/-}$ mice were stimulated by plate-coated anti-CD3/CD28 Abs (1 μg/ml) in the presence of IgG or recombinant mouse IL-12 (1 ng/ml) for 3 day. Then IFN-γ production was detected with FACS gated on CD3$^+$CD8$^+$ cells. Date shown represent one of two experiments with similar results. (**c**) Naïve CD8 T cells were stimulated by PMA (50 ng/ml) and Ionomycin (1 μg/ml) or by plate-coated anti-CD3/CD28 Abs (1 μg/ml) for different times as indicated. Total RNA was extracted. IFN-γ and TNF mRNA levels were detected by qRT-PCR. The qRT-PCR data were normalized relative to GAPDH mRNA levels and further normalized to the results from untreated group. Results shown are

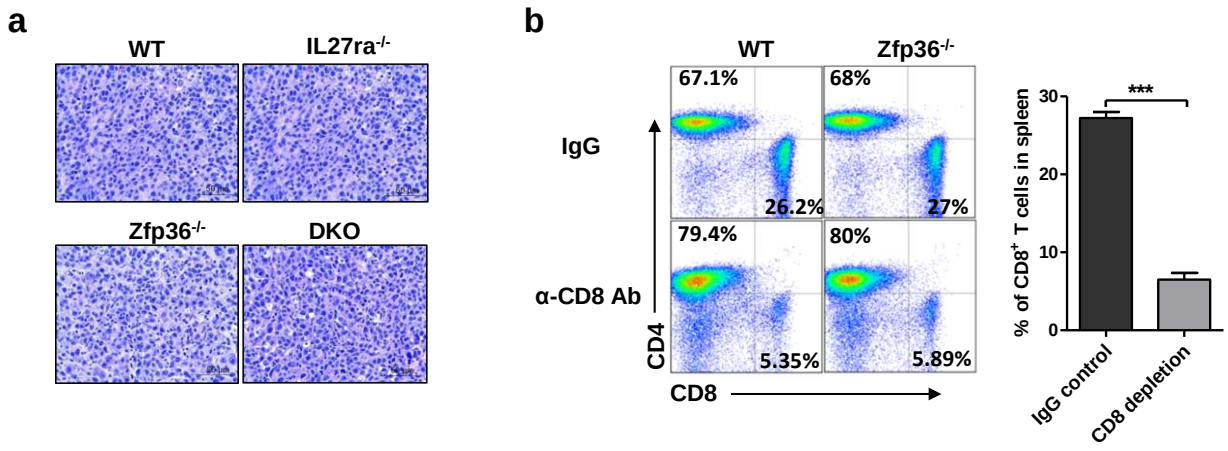
means ± s.e.m of three independent experiments. (**d**) Splenocytes of $CD4^{Cre}TTP^{+/+}$and $CD4^{Cre}TTP^{f/f}$ mice were stimulated by PMA and Ionomycin in the presence of GolGistop for 4h or by soluble anti-CD3/CD28 Abs (1 μg/ml) for different time points as indicated. IFN-γ production was detected with FACS by gating on $CD3^+CD8^+$ cells. The percentages and numbers of IFN-$\gamma^+$CD8 T cells in $CD8^+$ population were summarized from three independent experiments (means ± s.d.). (e) Splenocytes of $CD4^{Cre}TTP^{+/+}$and $CD4^{Cre}TTP^{f/f}$ mice were stained for CD3, CD8 and CD44. $CD44^+$ and $CD44^-$ cells were counted by gating on $CD3^+CD8^+$ population. The ratio of naïve to effector cells were calculated as $CD44^-$ cells vs. $CD44^+$ cells. Data shown are means ± s.d. of four experiments.



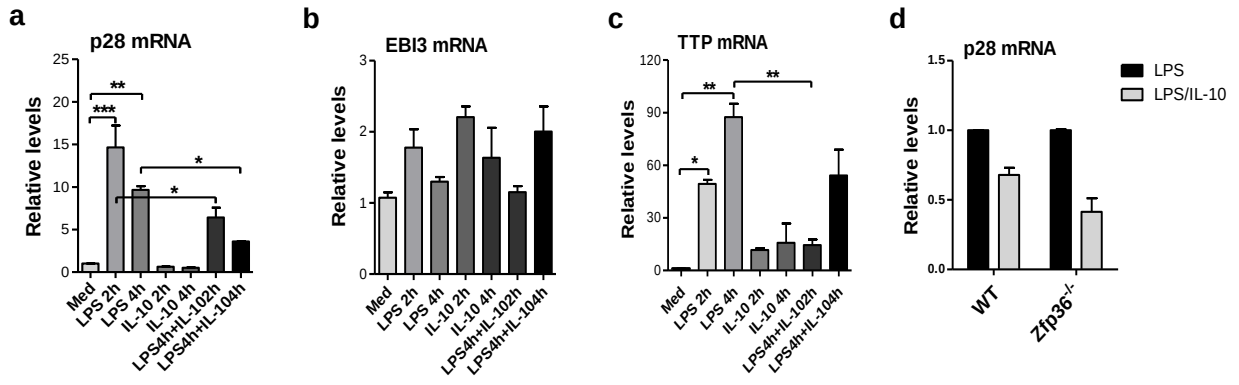

**Supplementary Fig. 3. IL-27 expression is increased in *Zfp36*$^{-/-}$ macrophages.** (**a,b**) p28 and EBI3 mRNA in liver and lung of WT and *Zfp36*$^{-/-}$ mice were detected by qRT-PCR and normalized relative to GAPDH mRNA levels and further normalized to the results from WT mice. Results shown are means ± s.e.m of five mice in each group and analyzed with unpaired Students' *t* test. (**c**) BMDM derived bone marrow cells of WT and *Zfp36*$^{-/-}$ mice were stimulated by LPS for 4 h. Then, p28 and EBI3 mRNA, and IL-27 protein were detected by qRT-PCR and ELISA, respectively (n=3). (**d**) J774 cells were infected by control/adenovirus (Ctrl/Ad) or TTP/adenovirus (TTP/Ad) for 48 h, and then stimulated by LPS for 4 h. The mRNAs of TTP, p28 and EBI3 were detected by qRT-PCR. Data shown are means ± s.e.m. from three independent experiments and analyzed with unpaired Students'*t* test. *: $p<0.05$; **: $p<0.01$; ***: $p<0.001$.




**Supplementary Fig.4. IL-27 derived from *Zfp36*$^{-/-}$ macrophages enhances IFN-γ production by CD8 T cells.** (**a**) WT and *Zfp36*$^{-/-}$ peritoneal macrophages were stimulated by LPS (1 μg/ml) for 24 h, and then supernatants were collected. Purified naïve WT and *IL27ra*$^{-/-}$ CD8$^{+}$ T cells were cultured with the supernatants (1:1) in the presence of plate-coated α-CD3/CD28 Abs (1 μg/ml) for 3 days. The percentages of IFN-γ$^{+}$CD8$^{+}$T cells were detected by FACS and shown as means ± s.d. from three independent experiments. (**b**) Supernatants of the *Zfp36*$^{-/-}$ peritoneal macrophages were respectively pre-treated with TNF and IL-23 neutralizing antibodies (10 μg/ml) for 30 min, and then cultured with WT naïve CD8 T cells (supernatant vs. medium=1:1) in the presence of plate-coated α-CD3/CD28 Abs (1 μg/ml) for 3 days. IFN-γ$^{+}$CD8$^{+}$T cells were detected by FCM. Quantitative data shown are means ± s.d. from three independent experiments. One-way ANOVA with Turkey was used as in (a & b), *: $p$<0.05; **: $p$<0.01; ***: $p$<0.001 between groups.




**Supplementary Fig. 5. TTP-mediated tumor progression is dependent on CD8 T cells.** (**a**) $0.5\times10^6$ EO771 cells were inoculated into mammary gland pads of WT, *IL27ra*$^{-/-}$, *Zfp36*$^{-/-}$, and DKO mice. Twenty-four days after tumor cell inoculation, mice were sacrificed and tumors were analyzed with HE staining (magnification 100×). (**b**) Splenocytes purified from the tumor-bearing mice receiving CD8 depletion antibody as in Fig. 6j were stained with antibodies against CD3, CD4 and CD8, then detected by FACS. The percentages of $CD4^+$ and $CD8^+$ T cells were determined by gating on $CD3^+$ cells. Bar shows means ± s.d. with four samples in each group (unpaired Student's *t* test, ***: $p<0.001$).




**Supplementary Fig. 6. IL-10 inhibits IL-27 production independent of TTP.** (**a-c**) BMDMs of WT mice were stimulated by LPS (1 μg/ml), recombinant mouse IL-10 (10 ng/ml), or combination of both for 2 and 4 hrs, respectively. The mRNA levels of IL-27 p28 (**a**), EBI3 (**b**) and TTP (**c**) were detected by qRT-PCR. The qRT-PCR data were normalized relative to GAPDH mRNA levels and further normalized to the results from untreated group (Med). Results shown are means ± s.e.m of three independent experiments and analyzed with one-way ANOVA (Nonparametric) with Tukey (compare all pairs of columns). (**d**) BMDMs of WT and *Zfp36*$^{-/-}$ mice were stimulated by LPS (1 μg/ml) with or without IL-10 (40 ng/ml) for 2h. Then p28 mRNA was detected by qRT-PCR. Results shown are means ± s.d. of three independent experiments and analyzed with unpaired two-tailed Student's *t* test. *: $p<0.05$; **: $p<0.01$; ***: $p<0.001$ between indicated groups.

**Supplementary Table l. Antibody list**

| Name | Company | Catalog number | Clone number |
|---|---|---|---|
| Anti-Mouse CD3 APC-780 | eBioscience | 47-0032-82 | 17A2 |
| Anti-Mouse CD3 Percp-cy5.5 | Biolegend | 100217 | 17A2 |
| Anti-Mouse CD4 percp | BD Biosciences | 553052 | RM4-5 |
| Anti-Mouse CD8 FITC | eBioscience | 11-0081-82 | 53-6.7 |
| Anti-Mouse CD8 PE | BD Biosciences | 552877 | 53-6.7 |
| Anti-Mouse CD8 APC-780 | eBioscience | 47-0032-82 | 53-6.7 |
| Anti-Mouse IFN-γ APC | BD Biosciences | 554413 | XMG1.2 |
| Anti-Mouse IL-2 FITC | eBioscience | 11-7021-41 | JES6-5H4 |
| Anti-mouse TNF-α FITC | eBioscience | 11-7321-81 | MP6-XT22 |
| Anti-mouse Granzyme B PE-CY7 | eBioscience | 25-5831-82 | GzA-3G8.5 |
| Anti-mouse Perforin APC | eBioscience | 17-9392-80 | eBioOMAK-D |
| Anti-mouse CD25 PE | eBioscience | 12-0251-81 | PC61.5 |
| Anti-mouse CD69 Percy-cy5.5 | eBioscience | 45-0691-80 | H1.2F3 |
| Anti-Human/Mouse CD44 FITC | eBioscience | 11-0441-81 | IM7 |
| Anti-Mouse CD62L | BD Biosciences | 560516 | MEL-14 |
| Anti-mouse Ki-67 PE | Biolegend | 652404 | 16A8 |
| Anti-Mouse CD8a Purified | eBioscience | 14-0081-82 | 53-6.7 |
| Anti-Mouse CD45 PE-cy7 | eBioscience | 25-0451 | 30-F11 |
| Anti-TTP (N-terminal) | Sigma | T5327 | polyclonal |
| Anti-mouse IL-12/IL-23 p40 | Biolegend | 505304 | C17.8 |
| Anti-mouse IL-23 p19 | Biolegend | 513805 | MMp19B2 |
| Anti-mouse TNF-α | eBioscience | 14-7423-85 | TN3-19.12 |
| Anti-mouse CD8α | Bio X cell | BP0004-1 | 53-6.7 |